REMARKS/ARGUMENTS

Claims 1-2, 4-6, and 8-10 are presently pending, while Claim 3 and 14 have been canceled. Support for the claim amendments can be found within the existing claims and support for Claim 4 is found on page 1, line 18; and page 64, line 24 of the Specification. No new matter has been added. Canceled and amended subject matter should not be considered abandoned, since Applicants reserve the right to file subsequent applications pursuing such subject matter.

As requested, Applicants have provided a new title for the Specification and also have amended Claim 5 to include a comma between the word "primate" and the word "porcine".

Applicants appreciate the Examiner's withdrawal of a number of the prior rejections in view of Applicants' response. An Information Disclosure Statement was filed by Applicants on September 24, 2007, so they would appreciate an acknowledgement from the Examiner with the next communication.

Rejection under 35 USC §112, first paragraph, enablement

All of the claims of the present application have been rejected under 35 USC §112, first paragraph, for allegedly being non-enabling. Applicants respectfully traverse.

On page 4, the Office Action states that the Specification does not provide enablement with respect to four aspects:

1) a method of detecting or isolating any stem cell other than a mammalian stem cell undergoing differentiation;

2) a method of detecting or isolating stem cells wherein the absence of 5T4 antigen expression indicates undifferentiated stem cells;

3) any method of detecting or isolating stem cells undergoing differentiation that uses a means of detection other than a 5T4 antigen antibody; and

4) any method of detecting or separating a differentiated stem cell."

These issues will be addressed in turn.

With regard to issue 1), the Examiner states that mammalian stem cells are enabled. Since Applicants have amended the claims to include mammalian embryonic stem cells, they respectfully request that the rejection with respect to issue 1) be withdrawn.

As to issue 2), all of the claims require the detection of the expression of 5T4 antigen to indicate the cells undergoing differentiation, except for Claim 2, which is directed to undifferentiated stem cells. In support of the Office's position that "a lack of a differentiation marker does not necessary [sic] indicate that the stem cells are not undergoing differentiation or is not a differentiated cell", the reference Ward is cited. Applicants respectfully point out that the markers of Ward, TTR, NF-68 and fgf-5, are germ-layer specific markers and the absence of one of those markers indicates only that the stem cell is not of that specific germ-layer lineage and does not necessarily indicate that the stem cell is not undergoing differentiation or is not a differentiated cell. 5T4 antigen is not a germ-layer-specific marker, but is an earlier marker of stem cells undergoing differentiation.

Applicants have shown that undifferentiated stem cells lack 5T4 antigen at the cell surface. Starting with embryonic stem cells that are known to be pluripotent, and culturing them under conditions known to maintain them in an undifferentiated, pluripotent state, which includes retaining the expression of OCT-4, a marker known to indicated undifferentiated integrity, Applicants have shown these cells lack 5T4 antigen on their surface. See Figure 12a.

See also Figures 20 and 21, wherein cells of the pluripotent GCT 27 and GCT 35 lines are 5T4 negative when grown in undifferentiated culture conditions (grown on pefs). Also, see Figures 24-27 wherein 5T4 expression is not associated with stem cells expressing OCT-4.

Furthermore, when stem cells were sorted for expression of SSEA1 (a known marker of undifferentiated stem cells), it was shown that cells lacking 5T4 antigen on their cell surfaces have a better efficiency of chimera formation (measure of pluripotentcy), than do cells that express 5T4 on the cell surface. In conclusion, the lack of 5T4 antigen on the cell surface is a better marker of undifferentiated pluripotent cells than is the marker SSEA1. For these reasons, Applicants assert that the Specification does establish that the absence of 5T4 antigen is correlated with undifferentiated cells.

Regarding issue 3), most of the claims detect the stem cells undergoing differentiation using an anti- 5T4 antibody and therefore, the rejection does not apply to those claims. Only Claim 1 does not specify the way the expression of 5T4 is determined. Please note, however, that Claim 1 has been amended to indicate that the 5T4 expression is on the cell surface.

Applicants assert that one of skill in the art would be able to utilize other methods of detection in addition to the use of antibodies. For example, one could isolate the 5T4 antigen protein from the cell to indicate its presence, which would not require the use of antibodies. Just because the use of antibodies may be the preferable approach, it does not follow that other routes would not be available.

The Specification provides an extensive discussion of methods to detect 5T4 antigen expression, starting on page 15, line 25, through page 20. The expression of 5T4 can be measured by gene transcription via mRNA, by RT-PCR, by probes, by FACS sorting, and by protein expression, including the use of antibodies, as well as by

intracellular partners for 5T4. These various routes are known to those of skill in the art and as a result, Claim 1 is properly enabled.

Issue 4) relates to the methods for detecting or separating a differentiated stem cell. Although Applicants disagree with the Office's premise that a skilled artisan would not know how to detect or isolate differentiated stem cells, they have amended the claims to provide that the cells being detected are those undergoing differentiation. For these reasons, issue 4) has been overcome and all aspects of the enablement rejection should be withdrawn.

Rejection under 35 USC §112, second paragraph

Claims 2, 8, 9, and 14 have been rejected as allegedly indefinite due to the phrase "differentiated stem cells". It is noted that Claim 14 has been canceled and Claim 2 does not contain the phrase; thus, the rejection should be withdrawn as to these claims. Applicants have amended Claims 8 and 9 to recite that the cells are undergoing differentiation. Based upon this amendment, Applicants request withdrawal of the remaining rejection.

Claim 9 has been rejected as allegedly indefinite due to the limitation "the cells" in step c lacking antecedent basis. Dependent Claim 10 as been rejected by association. Applicants have amended Claim 9 to include "isolating either the bound or unbound cells" in step c. As a result, they request the withdrawal of the rejection of Claims 9 and 10.

Claim 14 has been rejected as allegedly being indefinite due to a gap between steps for the "use of an antibody". Applicants have canceled this claim, thereby rendering the rejection moot.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-350-6108.

Respectfully submitted,

Karen Babyak-Dow

Karen B. Dow
Reg. No. 29,684

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 858-350-6100
Fax: 415-576-0300
KBD:tro

61211185 v1